# A Case Report of Delayed Respiratory Depression in Epidural Opioids

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## Introduction

The popularity of epidural opioids has increased since the 1980's[1]. The advantages of epidural opioids are that of profound segmental antinociception. This level of antinociception can be achieved with smaller doses than used systemically and without added motor, sensory, or autonomic blockade of local anesthetics[1]. While the use of epidural opioids has increased as a result of the intense antinociception a variety of non-nociceptive side effects have become evident. The four most common side effects are pruritis, nausea and vomiting, urinary retention, and respiratory depression. Respiratory depression is the most serious side effect and has been differentiated as early and late. Early occurs within two hours of opioid administration and results from systemic absorption. The blood concentration of the opioid is proportional to the magnitude of respiratory depression[2]. Delayed respiratory depression occurs greater than two hours after opioid administration; characteristically at 6-12 hours and the patient may be at risk for up to 24 hours post opioid administration [3]. Delayed respiratory depression results from cephalad spread of opioid in cerebrospinal fluid and subsequent interaction with opioid receptors located in the ventral medulla[3].

The following is a case report of a patient, status post a total knee replacement, who experienced delayed respiratory depression while receiving epidural opioids.

## Case Summary

A 61-year-old, 122 kg, Caucasian female presented for a left total knee replacement. The preoperative anesthesia assessment revealed an ASA II female. The patient's medical history revealed Parkinson's disease, gastroesophageal reflux, depression, and obesity. Medications consisted of levadopa (50 mg twice a day), prilosec

(20 mg once a day), and trazadone (200 mg once a day). The previous surgical history included 2 previous total knee replacements of the right knee. There was no history of anesthetic complications.

The patient consented to a continuous lumbar epidural for the primary anesthetic with intravenous sedation as needed. Premedication for aspiration risk included bicitra 30 mL by mouth, zofran 4 mg, and zantac 50 mg intravenously. The epidural was easily placed at lumbar interspaces 3-4 and a sensory block level at thoracic level 8 was achieved. This level was maintained with 3 mL bolus of 2% lidocaine with 1:200,000 epinephrine and bicarbonate approximately every 30 minutes. In addition 2 doses of epidural fentanyl was administered 50 mcg prior to incision and 25 mcg approximately 2 ¾ hours after the original dose. Total intravenous sedation given intraoperatively included versed 6.5 mg and fentanyl 100 mcg over 5 ½ hours. Upon arrival in the recovery room the patient had a T12 sensory level and was placed on a continuous epidural infusion of bupivicaine 1/8% with hydromorphone 20mcg/ml at 6mLs/hour.

Approximately 30 minutes into the PACU stay the patient complained of pain with a visual acuity score (VAS) of 7/10. The epidural was again bloused with fentanyl 50mcg and the infusion was increased to 9mLs/hour. Total time spent in PACU was 2 hours; the patient remained stable and was transferred to a surgical ward with a VAS of <1/10.

Approximately 7 hours postoperatively, the patient became significantly somulent, and was not responsive to verbal stimuli. The vital signs revealed a respiratory rate of 10 breaths per minute, oxygen saturation in the 70's, blood pressure of 118/51 mmHg, and heart rate of 118 BPM. An arterial blood gas was drawn and the results were

consistent with a respiratory acidosis (pH 7.22, paCO2 78 mmHg, pO2 60mmHg, HCO3 32mmol/L, BE 4 mmol/L, and s02 82%). The patient was administered naloxone 0.6 mg intravenously and immediately became responsive to verbal stimuli. The respiratory rate improved to 14 breaths per minute and the O2 sat increased to 99%. The continuous epidural infusion was changed to bupivicaine 1/8% at 6mLs/hour without narcotics and the patient was transferred to PACU for close observation over night.

The patient remained stable throughout the night and was transferred back to the surgical ward. The epidural was discontinued at 24 hours postoperative and physical therapy started. She was discharged to home on postoperative day 4.

**Discussion**

Side effects of epidural opioids are caused by the presence of the drug in either the cerebral spinal fluid or the blood. The propensity of epidural opioids to cause side effects, particularly respiratory depression, is largely related to the dose and the pharmacokinetics of the specific opioid[4]. The epidural space contains an extensive venous plexus and vascular reabsorption is extensive. A highly lipid soluble drug is absorbed relatively quickly and although accumulation and cephalad spread is uncommon, a high blood concentration is more likely to occur and increase the risk of early respiratory depression[4]. Thus, early respiratory depression is likely to occur when using such opioids as fentanyl and sufentanil. The less lipid soluble opioids, morphine and hydromorphone, tend to accumulate and cephalad spread of the opioid occurs with bulk flow of cerebrospinal fluid as it diffuses through the dura, which can increase the risk of delayed respiratory depression[1].

Although dose and pharmacokinetics play a large role in the extent of side effects there are other contributing factors. The obese, elderly, and pregnant patient may have exaggerated cephalad spread and require decrease doses[5]. Nishimura, Kitahara, and Kusakabe documented cephalad spread of lidocaine in patients over 50 years suggesting that decreased volumes of epidural agents be used in this population[6]. Bromage also suggested that the anatomical changes that occur in the elderly epidural space causes cephalad spread[7]. Cephalad spread may also be exaggerated in cases of increased intrathoracic pressure for example coughing or grunting as seen in abdominal or thoracic pain[4]. Concomitant use of other opioids and sedatives cause synergistic effects and increase risk for respiratory depression.

In the case report above the patient experienced delayed respiratory depression. The cause was multifactorial; she was an obese, elderly patient receiving a continuous infusion of a less lipid soluble opioid. In reviewing the use of epidural opioids in the literature, the advantages of their use supersedes the possible side effects that can occur. While it is true that the aforementioned side effects are more common with intrathecal opioids the probability of their occurrence in epidural opioids is clinically relevant and warrants close observation[1]. The respiratory depression is of the most serious side effects and one must vigilantly monitor for the signs and systems in order to avoid devastating events.

## References


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